

attcggtctcg agttcacctg gtgctgcttt gacttcaggc tcttccttct gccagctcc	60
gtcccaccca gcagcccgca gagnaaggag gcagctggca ccacactggg ctttggagac	120
actgcgggga ctgtggaccc caccctgctg cacggagctc ctgcaaaagc aaacctgaga	180
accttgggtc ctcccagcgc ccagcc atg ggg gaa ctg tgc tgc agc gac tcc	233
Met Gly Glu Leu Cys Arg Arg Asp Ser	
1 5	
gca ctc acg gca ctg gac gag gag aca ctg tgg gag atg atg gag agc	281
Ala Leu Thr Ala Leu Asp Glu Glu Thr Leu Trp Glu Met Met Glu Ser	
10 15 20 25	
cac cgc cac agg atc gta cgc tgc atc tgc ccc agc cgc ctc acc ccc	329
His Arg His Arg Ile Val Arg Cys Ile Cys Pro Ser Arg Leu Thr Pro	
30 35 40	
tac ctg cgc cag gcc aag gtg ctg tgc cag ctg gac gag gag gag gtg	377
Tyr Leu Arg Gln Ala Lys Val Leu Cys Gln Leu Asp Glu Glu Glu Val	
45 50 55	
ctg cac agc ccc cgg ctc acc aac agc gcc atg cgg gcc ggg cac ttg	425
Leu His Ser Pro Arg Leu Thr Asn Ser Ala Met Arg Ala Gly His Leu	
60 65 70	
ctg gat ttg ctg aag act cga ggg aag aac ggg gcc atc gcc ttc ctg	473
Leu Asp Leu Leu Lys Thr Arg Gly Lys Asn Gly Ala Ile Ala Phe Leu	
75 80 85	
gag agc ctg aag ttc cac aac cct gac gtc tac acc ctg gtc acc ggg	521
Glu Ser Leu Lys Phe His Asn Pro Asp Val Tyr Thr Leu Val Thr Gly	
90 95 100 105	
ctg cag cct gat gtt gac ttc agt aac ttt agc ggt ctc atg gag aca	569
Leu Gln Pro Asp Val Asp Phe Ser Asn Phe Ser Gly Leu Met Glu Thr	
110 115 120	
tcc aag ctg acc gag tgc ctg gct ggg gcc atc ggc agc ctg cag gag	617
Ser Lys Leu Thr Glu Cys Leu Ala Gly Ala Ile Gly Ser Leu Gln Glu	
125 130 135	
gag ctg aac cag gaa aag ggg cag aag gag gtg ctg ctg cgg cgg tgc	665
Glu Leu Asn Gln Glu Lys Gly Gln Lys Glu Val Leu Leu Arg Arg Cys	
140 145 150	
cag cag ctg cag gag cac ctg ggc ctg gcc gag acc cgt gcc gag ggc	713
Gln Gln Leu Gln Glu His Leu Gly Leu Ala Glu Thr Arg Ala Glu Gly	
155 160 165	
ctg cac cag ctg gag gct gac cac agc cgc atg aag cgt gag gtt agc	761
Leu His Gln Leu Glu Ala Asp His Ser Arg Met Lys Arg Glu Val Ser	
170 175 180 185	
gca cac ttc cat gag gtg ctg agg ctg aag gac gag atg ctc agc ctc	809
Ala His Phe His Glu Val Leu Arg Leu Lys Asp Glu Met Leu Ser Leu	
190 195 200	

Fig. 1A

tcg ctg cac tat agc aat gcg ctg cag gag aag gag ctg gcc gcc tca	857
Ser Leu His Tyr Ser Asn Ala Leu Gln Glu Lys Glu Leu Ala Ala Ser	
205 210 215	
cgc tgc cgc agc ctg cag gag gag ctg tat cta ctg aag cag gag ctg	905
Arg Cys Arg Ser Leu Gln Glu Glu Leu Tyr Leu Leu Lys Gln Glu Leu	
220 225 230	
cag cga gcc aac atg gtt tcc tcc tgt gag ctg gaa ttg caa gag cag	953
Gln Arg Ala Asn Met Val Ser Ser Cys Glu Leu Glu Leu Gln Glu Gln	
235 240 245	
tcc ctg agg aca gcc agc gac cag gag tcc ggg gat gag gag ctg aac	1001
Ser Leu Arg Thr Ala Ser Asp Gln Glu Ser Gly Asp Glu Glu Leu Asn	
250 255 260 265	
cgc ctg aag gag gag aat gag aaa ctg cgc tcg ctg act ttc agc ctg	1049
Arg Leu Lys Glu Glu Asn Glu Lys Leu Arg Ser Leu Thr Phe Ser Leu	
270 275 280	
gcg gag aag gac att ctg gag cag agc ctg gac gag gcg cgg ggg agc	1097
Ala Glu Lys Asp Ile Leu Glu Gln Ser Leu Asp Glu Ala Arg Gly Ser	
285 290 295	
cga cag gag ctg gtg gag cgc atc cac tcg ctg cgg gag cgg gcc gtg	1145
Arg Gln Glu Leu Val Glu Arg Ile His Ser Leu Arg Glu Arg Ala Val	
300 305 310	
gct gcc gag agg cag cga gag cag tac tgg gaa gag aag gaa cag acc	1193
Ala Ala Glu Arg Gln Arg Glu Gln Tyr Trp Glu Glu Lys Glu Gln Thr	
315 320 325	
ctg ctg cag ttc cag aag agt aag atg gcc tgc caa ctc tac agg gag	1241
Leu Leu Gln Phe Gln Lys Ser Lys Met Ala Cys Gln Leu Tyr Arg Glu	
330 335 340 345	
aag gtg aat gcg ctg cag gcc cag gtg tgc gag ctg cag aag gag cga	1289
Lys Val Asn Ala Leu Gln Ala Gln Val Cys Glu Leu Gln Lys Glu Arg	
350 355 360	
gac cag gcg tac tcc gcg agg gac agt gct cag agg gag att tcc cag	1337
Asp Gln Ala Tyr Ser Ala Arg Asp Ser Ala Gln Arg Glu Ile Ser Gln	
365 370 375	
agc ctg gtg gag aag gac tcc ctc cgc agg cag gtg ttc gag ctg acg	1385
Ser Leu Val Glu Lys Asp Ser Leu Arg Arg Gln Val Phe Glu Leu Thr	
380 385 390	
gac cag gtc tgc gag ctg cgc aca cag ctt cgc cag ctg cag gca gag	1433
Asp Gln Val Cys Glu Leu Arg Thr Gln Leu Arg Gln Leu Gln Ala Glu	
395 400 405	
cct ccg ggt gtg ctc aag cag gaa gcc agg acc agg gag ccc tgt cca	1481
Pro Pro Gly Val Leu Lys Gln Glu Ala Arg Thr Arg Glu Pro Cys Pro	
410 415 420 425	

cgg gag aag cag cgg ctg gtg cgg atg cat gcc atc tgc ccc aga gac	1529
Arg Glu Lys Gln Arg Leu Val Arg Met His Ala Ile Cys Pro Arg Asp	
430 435 440	
gac agc gac tgc agc ctc gtc agc tcc aca gag tct cag ctc ttg tcg	1577
Asp Ser Asp Cys Ser Leu Val Ser Ser Thr Glu Ser Gln Leu Leu Ser	
445 450 455	
gac ctg agt gcc acg tcc agc cgc gag ctg gtg gac agc ttc cgc tcc	1625
Asp Leu Ser Ala Thr Ser Ser Arg Glu Leu Val Asp Ser Phe Arg Ser	
460 465 470	
agc agc ccc gcg ccc ccc agc cag cag tcc ctg tac aag cgg gtg gcc	1673
Ser Ser Pro Ala Pro Pro Ser Gln Gln Ser Leu Tyr Lys Arg Val Ala	
475 480 485	
gag gac ttc ggg gaa gaa ccc tgg tct ttc agc agc tgc ctg gag atc	1721
Glu Asp Phe Gly Glu Glu Pro Trp Ser Phe Ser Ser Cys Leu Glu Ile	
490 495 500 505	
ccg gag gga gac ccg gga gcc ctg ccg gga gct aag gca ggc gac cca	1769
Pro Glu Gly Asp Pro Gly Ala Leu Pro Gly Ala Lys Ala Gly Asp Pro	
510 515 520	
cac ctg gat tat gag ctc cta gac acg gca gac ctt ccg cag ctg gaa	1817
His Leu Asp Tyr Glu Leu Leu Asp Thr Ala Asp Leu Pro Gln Leu Glu	
525 530 535	
agc agc ctg cag cca gtc tcc cct gga agg ctt gat gtc tcg gag agc	1865
Ser Ser Leu Gln Pro Val Ser Pro Gly Arg Leu Asp Val Ser Glu Ser	
540 545 550	
ggc gtc ctc atg cgg cgg agg cca gcc cgc agg atc ctg agc cag gtc	1913
Gly Val Leu Met Arg Arg Arg Pro Ala Arg Arg Ile Leu Ser Gln Val	
555 560 565	
acc atg ctg gcg ttc cag ggg gat gca ttg ctg gag cag atc agc gtc	1961
Thr Met Leu Ala Phe Gln Gly Asp Ala Leu Leu Glu Gln Ile Ser Val	
570 575 580 585	
atc ggc ggg aac ctc acg ggc atc ttc atc cac cgg gtc acc ccg ggc	2009
Ile Gly Gly Asn Leu Thr Gly Ile Phe Ile His Arg Val Thr Pro Gly	
590 595 600	
tcg gcg gcg gac cag atg gcc ttg cgc ccg ggc acc cag att gtg atg	2057
Ser Ala Ala Asp Gln Met Ala Leu Arg Pro Gly Thr Gln Ile Val Met	
605 610 615	
gtt gat tac gaa gcc tca gag ccc ttg ttc aag gca gtc ctg gag gac	2105
Val Asp Tyr Glu Ala Ser Glu Pro Leu Phe Lys Ala Val Leu Glu Asp	
620 625 630	
acg acc ctg gag gag gcc gtg ggg ctt ctc agg agg gtg gac ggc ttc	2153
Thr Thr Leu Glu Glu Ala Val Gly Leu Leu Arg Arg Val Asp Gly Phe	
635 640 645	

Fig. 1C

tgc tgc ctg tct gtg aag gtc aac acg gac ggt tat aag agg cta ctc	2201
Cys Cys Leu Ser Val Lys Val Asn Thr Asp Gly Tyr Lys Arg Leu Leu	
650 655 660 665	
cag gac ctg gag gcc aaa gtg gcg acc tcg ggg gac tca ttc tac atc	2249
Gln Asp Leu Glu Ala Lys Val Ala Thr Ser Gly Asp Ser Phe Tyr Ile	
670 675 680	
cgg gtc aac ctg gcc atg gag ggc agg gcc aaa ggg gag ctg cag gtg	2297
Arg Val Asn Leu Ala Met Glu Gly Arg Ala Lys Gly Glu Leu Gln Val	
685 690 695	
cat tgc aac gag gtc ctg cac gtc acc gac acc atg ttc cag ggc tgc	2345
His Cys Asn Glu Val Leu His Val Thr Asp Thr Met Phe Gln Gly Cys	
700 705 710	
ggc tgc tgg cat gcc cac cgc gtg aac tct tac acc atg aag gat act	2393
Gly Cys Trp His Ala His Arg Val Asn Ser Tyr Thr Met Lys Asp Thr	
715 720 725	
gcc gcg cac ggc acc atc ccc aac tac tcc agg gct cag cag cag ctc	2441
Ala Ala His Gly Thr Ile Pro Asn Tyr Ser Arg Ala Gln Gln Gln Leu	
730 735 740 745	
ata gcc ctc atc cag gac atg act cag cag tgc acc gtg acc cgc aag	2489
Ile Ala Leu Ile Gln Asp Met Thr Gln Gln Cys Thr Val Thr Arg Lys	
750 755 760	
cca tct tct ggg gga cca cag aag ctg gtc cgc atc gtc agt atg gac	2537
Pro Ser Ser Gly Gly Pro Gln Lys Leu Val Arg Ile Val Ser Met Asp	
765 770 775	
aaa gcc aag gcc agc cct ctg cgt ttg tcc ttt gac agg ggc cag ttg	2585
Lys Ala Lys Ala Ser Pro Leu Arg Leu Ser Phe Asp Arg Gly Gln Leu	
780 785 790	
gac ccc agc agg atg gag ggc tcc agc acg tgc ttc tgg gcc gag agc	2633
Asp Pro Ser Arg Met Glu Gly Ser Ser Thr Cys Phe Trp Ala Glu Ser	
795 800 805	
tgc ctc acc ctg gtg ccc tat acc ctg gtg tgg ccc cat cga ccc gcc	2681
Cys Leu Thr Leu Val Pro Tyr Thr Leu Val Trp Pro His Arg Pro Ala	
810 815 820 825	
cgg ccc cgg cct gtg ctc ctc gtg ccc agg gcg gtt ggg aag atc ctg	2729
Arg Pro Arg Pro Val Leu Leu Val Pro Arg Ala Val Gly Lys Ile Leu	
830 835 840	
agc gag aaa ctg tgc ctc ctc caa ggg ttt aag aag tgc ctg gca gag	2777
Ser Glu Lys Leu Cys Leu Leu Gln Gly Phe Lys Lys Cys Leu Ala Glu	
845 850 855	
tac ttg agc cag gag gag tat gag gcc tgg agc cag aga ggg gac atc	2825
Tyr Leu Ser Gln Glu Glu Tyr Glu Ala Trp Ser Gln Arg Gly Asp Ile	
860 865 870	

Fig. 1D

atc cag gag gga gag gtg tcc ggg ggc cgc tgc tgg gtg acc cgc cat	2873
Ile Gln Glu Gly Glu Val Ser Gly Gly Arg Cys Trp Val Thr Arg His	
875 880 885	
gct gtg gag tcc ctc atg gaa aag aac acc cat gcc ctc ctg gac gtc	2921
Ala Val Glu Ser Leu Met Glu Lys Asn Thr His Ala Leu Leu Asp Val	
890 895 900 905	
cag ctg gac agt gtc tgc acc ctg cac agg atg gac atc ttc ccc atc	2969
Gln Leu Asp Ser Val Cys Thr Leu His Arg Met Asp Ile Phe Pro Ile	
910 915 920	
gtc atc cac gtc tct gtc aac gag aag atg gca aag aag ctc aag aag	3017
Val Ile His Val Ser Val Asn Glu Lys Met Ala Lys Lys Leu Lys Lys	
925 930 935	
ggc cta cag cgg ttg ggc acc tca gag gag cag ctc ctg gag gct gcg	3065
Gly Leu Gln Arg Leu Gly Thr Ser Glu Glu Gln Leu Leu Glu Ala Ala	
940 945 950	
agg cag gag gag gga gac ctg gac cgg gcg ccc tgt cta tac agc agc	3113
Arg Gln Glu Glu Gly Asp Leu Asp Arg Ala Pro Cys Leu Tyr Ser Ser	
955 960 965	
ctg gct cct gac ggc tgg agc gac ctg gac ggc ctg ctc agc tgt gtc	3161
Leu Ala Pro Asp Gly Trp Ser Asp Leu Asp Gly Leu Leu Ser Cys Val	
970 975 980 985	
cgc cag gcc atc gcc gac gag cag aag aag gtg gtg tgg acg gag cag	3209
Arg Gln Ala Ile Ala Asp Glu Gln Lys Lys Val Val Trp Thr Glu Gln	
990 995 1000	
agc ccc cga tga tgcaccgtgc cccttcccgg gactgtgggg gcttctgtgt	3261
Ser Pro Arg *	
gcctgttaat gcagtccctgt tcctcagccc aggccctctt ggcacagctg tgggctcctt	3321
ggcacatgag gccggctctc cccactggct ggggtctaac cttgaaccct caccacgtgc	3381
aggtcacaca cagtgaagcc acttgtaact gcacactttt ctgtggaaac atcttcaccc	3441
tttaccaggc ttggcatggt ctgaactgga aaccctgaga atgtttctgc agtaggacag	3501
gagggacatc ttcccatgcc ttccctagaa ccggaggccc cggacttctc tggaaaaccg	3561
cctgtctgca ggccccgattc aaatctatgg gggctgcact tccctttttac attttgatgt	3621
gtcaaaggct tttggagtga ccaaaagcac agaggcagcg ggtggggcgc ctgggtgggc	3681
cccaaggctg ctgccaccct tgcccggggc agaggcataa gccacatat gctgtgacgc	3741
tggccacctt ttctcagctt ctgaggctgc gatgcctcag gaactccagt ttacagagac	3801
cagtgtgttt acttgtaaat aaagcctctg ggtggtggag acggtacttt cagtgggtct	3861
gtgccccgtg gccccgtgtgc ctgttcggtg ggggtgtccc agagaagcct ggcaccagta	3921
ccccgtcaa	3931

Fig. 1E

V	E	S	L	M	E	K	N	T	H	A	L	L	D	V	Q	L	D	S	V	960
GTG	GAG	TCC	CTC	ATG	GAA	AAG	AAC	ACC	CAT	GCC	CTC	CTG	GAC	GTC	CAG	CTG	GAC	AGT	GTC	2880
C	T	L	H	R	M	D	I	F	P	I	V	I	H	V	S	V	N	E	K	980
TGC	ACC	CTG	CAC	AGG	ATG	GAC	ATC	TTC	CCC	ATC	GTC	ATC	CAC	GTC	TCT	GTC	AAC	GAG	AAG	2940
M	A	K	K	L	K	K	G	L	Q	R	L	G	T	S	E	E	Q	L	L	1000
ATG	GCA	AAG	AAG	CTC	AAG	AAG	GGC	CTA	CAG	CGG	TTG	GGC	ACC	TCA	GAG	GAG	CAG	CTC	CTG	3000
E	A	A	R	Q	E	E	G	D	L	D	R	A	P	C	L	Y	S	S	L	1020
GAG	GCT	GCG	AGG	CAG	GAG	GAG	GGA	GAC	CTG	GAC	CGG	GCG	CCC	TGT	CTA	TAC	AGC	AGC	CTG	3060
A	P	D	G	W	S	D	L	D	G	L	L	S	C	V	R	Q	A	I	A	1040
GCT	CCT	GAC	GGC	TGG	AGC	GAC	CTG	GAC	GGC	CTG	CTC	AGC	TGT	GTC	CGC	CAG	GCC	ATC	GCC	3120
D	E	Q	K	K	V	Q	R	R	R	H	P	R	I	N	P	S	Q	R	T	1060
GAC	GAG	CAG	AAG	AAG	GTG	CAA	CGC	CGA	CGT	CAT	CCA	AGA	ATT	AAC	CCA	AGC	CAG	AGG	ACG	3180
G	I	A	T	Q	Q	R	Q	C	H	R	R	I	N	P	R	Q	R	M	G	1080
GGC	ATC	GCC	ACC	CAG	CAA	CGC	CAG	TGT	CAC	CGA	AGA	ATT	AAC	CCA	AGG	CAG	AGG	ATG	GGC	3240
I	A	T	Q	Q	R	Q	C	H	R	R	I	N	P	S	Q	R	T	G	I	1100
ATT	GCC	ACC	CAG	CAA	CGC	CAG	TGT	CAC	CGA	AGA	ATT	AAC	CCA	AGC	CAG	AGG	ACG	GGC	ATC	3300
T	T	Q	Q	C	Q	C	H	R	R	I	N	P	S	Q	R	T	G	I	A	1120
ACC	ACC	CAG	CAA	TGC	CAG	TGT	CAC	CGA	AGA	ATT	AAC	CCA	AGC	CAG	AGG	ACG	GGC	ATC	GCC	3360
M	P	S	S	S	D	T	L	K	K	D	K	L	L	P	R	N	T	T		1139
ATG	CCT	TCA	TCT	TCG	GAC	ACT	CTC	AAA	AAA	GAT	AAG	CTT	CTG	CCC	AGA	AAC	ACC	ACA		3417

Fig. 2C

1.000

CARD DMR_positives_new CDRnew PSBds_new SHG_2 GAT_Guanidinate_in

1 40 80 120 160 200 240 280 320 360 400 440 480 520 560 600 640 680 720 760 800 840 880 920 960 1000 1040 1080 1120

Fig. 3

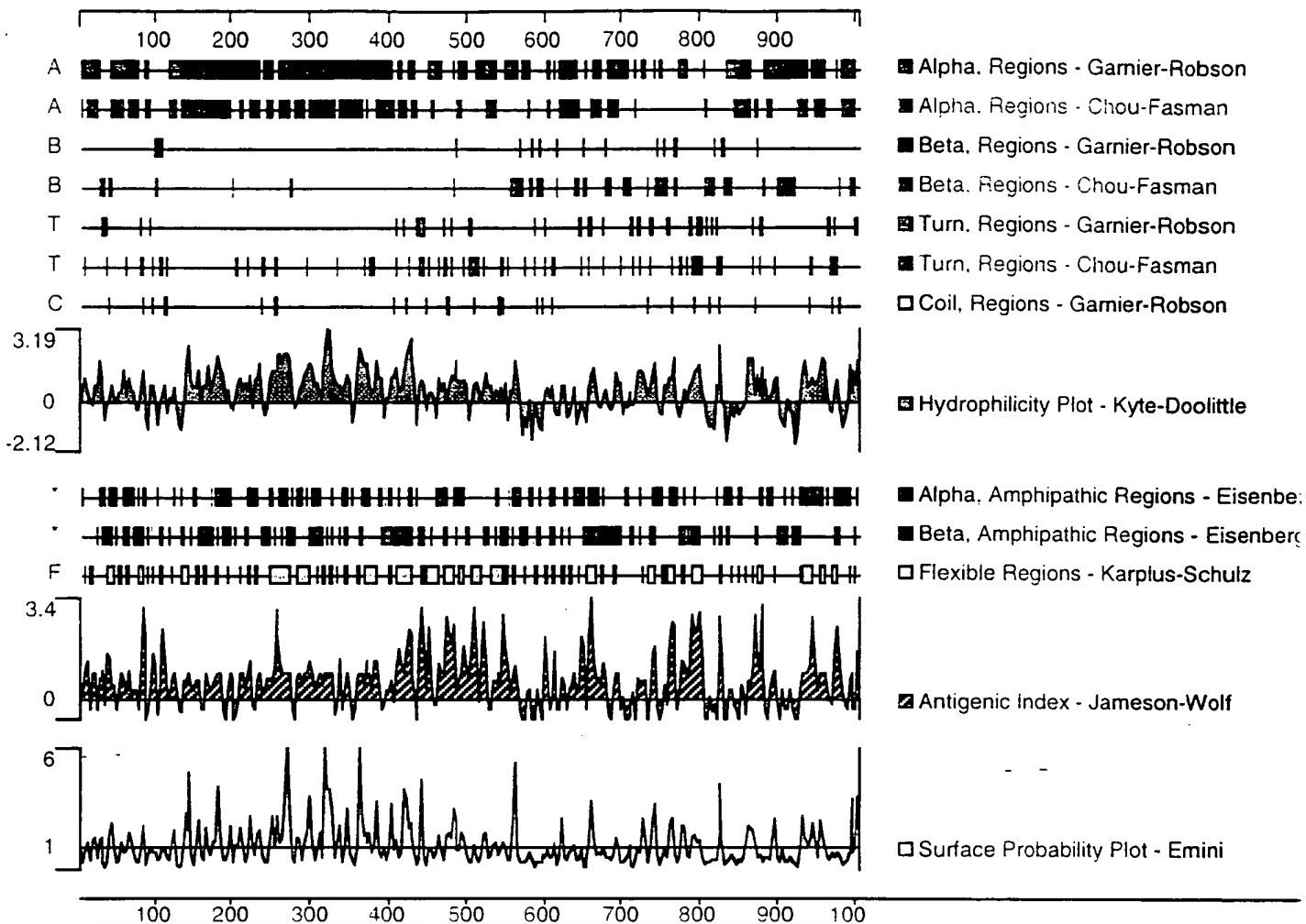


Fig. 4

[illegible]

CARD14 16 EETLWENTMESHRHRIVRCICPSRLTPYLROAKVLCQLDEEEVLHSPR 62

CARD14 63 LTNSaMRAGHLLDLLKTRGKNGAIAFLES LKFHNP DVYTLVTGLQ 107

Fig. 5A

PDZ domain 1 of 1, from 568 to 659: score 5.3, E = 0.39

PDZ: domain 1 of 1, from 568 to 659: score 5.3, E = 0.39

*->eitlekevkrsglGfsikggsdk..givvsevlpGsgaAeagGrLke

++t+ ++ l +i++ + + +gi++ +v pG +aA++ L++

CARD14 568 QVTMLAF-QGDALLEQISVIGGNltGIFIHRVTPG-SAADQMA-LRP 611

GDvIlsvNG.....qdvenmsheravlaiksgg..evtLtvIRd<-

G +I+ v+ + +++ + +e+ ++e+av +++ g ++++v d

CARD14 612 GTQIVMVDYeaseplfkAVLEDTTLEEAVGLLRVDGfcCLSVKVNTD 659

*

CARD14

Fig. 5B

SH3_2: domain 1 of 1, from 679 to 744: score -4.5, E = 3.8

*->eyvvAlYDyeagnedELsFkkGDiiTvleks..ddgWweGelnr...

+y ++ + e++ +EL ++ +++++v++ ++ g w + + ++ +

CARD14 679 FYIRVNLAMEGRAKGELOVHCNEVLHVTDTMfqGCGCWHHRVNsyt 725

...tGkeGlFpsnYVeeie<-*

++t G +P + ++

CARD14 726 mkdTAAHGtIPNYSRAQQQ 744

Fig. 5C

Guanylate_kin: domain 1 of 1, from 856 to 948: score -24.2, E = 0.073
 *->TRpVpRpgEvdGkdYhFVssrEemekdIaaneFlEygefqqnyYGTs
 CARD14 856 --A-----EYLS-QEEYEAWSQRGDIIQEGEVSGGRCWVT 887
 letvrqvakggKiciLDvepQgvkrlrtaelsNPivvFIaPpsl..qe
 CARD14 888 RHAVESLMEKNTHALLDVQLDSVCTLHRMDIF-PIVIHVSVNEKmakKLLK 936
 krLegrnkesEes<-*
 k L+++++ sEe+
 CARD14 937 KGLQRLGT-SEEQ 948

Fig. 5D

CARD14-CARD/AD



Fig. 6

Western blot analysis showing the expression of Myc-Card11 and Myc-Card14, and the interaction of Bcl10 with Myc-Card11. The blots are labeled as follows:

- WB: Bcl10**: Shows Bcl10 protein levels across six lanes.
- WB: Myc**: Shows Myc-Card11 and Myc-Card14 protein levels across six lanes.
- IP: Bcl10**: Shows Myc-Card11 and Myc-Card14 levels in Bcl10 immunoprecipitates across six lanes.
- WB: Myc**: Shows Myc-Card11 and Myc-Card14 protein levels in the immunoprecipitates across six lanes.

The lanes are numbered 1 to 6. The lanes are labeled as follows:

- 1**: + (Myc-Card11)
- 2**: - (Myc-Card11)
- 3**: + (Myc-Card14)
- 4**: - (Myc-Card14)
- 5**: - (control vector)
- 6**: + (control vector)

The blots show that Bcl10 interacts with Myc-Card11 but not with Myc-Card14. The control vector lanes (5 and 6) show no interaction.

Fig. 7

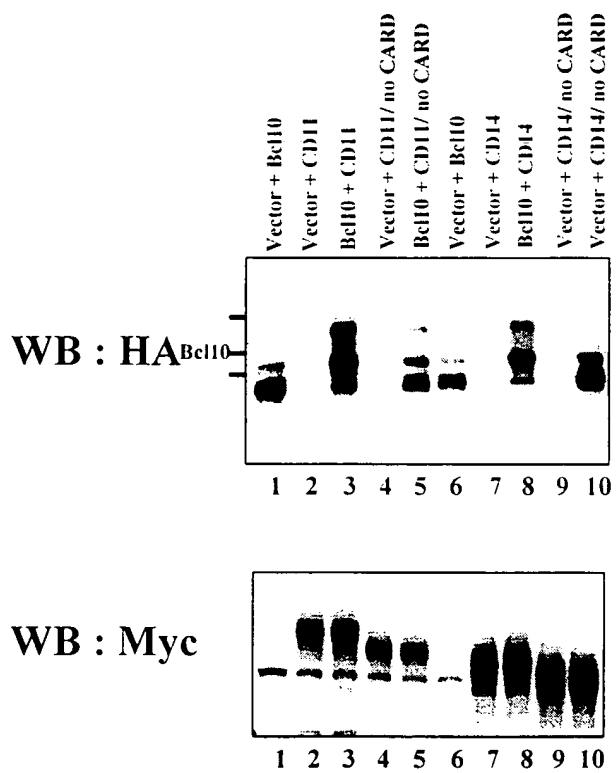


Fig. 8

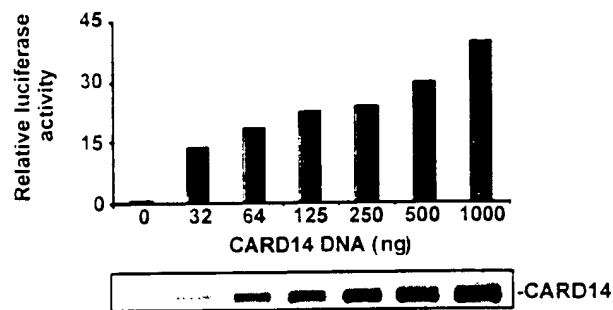


Fig. 9A

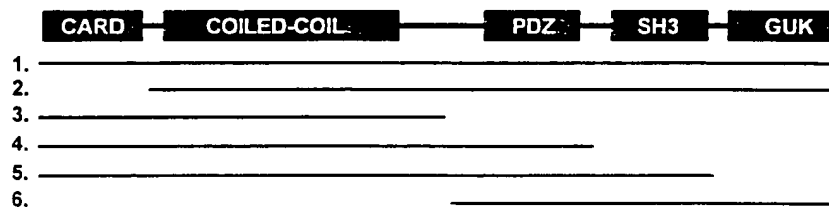


Fig. 9B

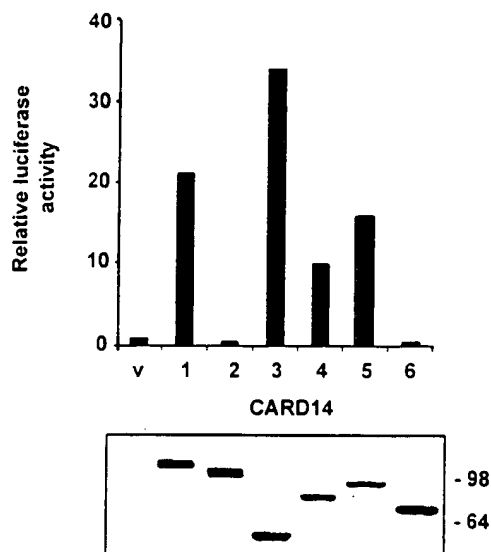


Fig. 9C